1	The Effect of Ethnicity on Left Ventricular Adaptation to Exercise
2	Authors: Jours Pagu ^a PMPCh MA DhD Chararda Einsschiars ^a MD DhD Christopher
2	Miles ⁴ DSe MDChD DhD Commo Domy Williams ⁴ MDChD Homish Mool ashlan ⁴ MDChD
4	Miles" BSc, MBCnB, PnD, Gemma Parry-williams" MBCnB, Hamish MacLachian" MBCnB,
5	MSc, Maite Tome" MD, PhD, Sanjay Sharma" BSc, MBChB, MD, Michael Papadakis"
6	MBBS, MD
7	
8	Institutions: ^a Cardiovascular Clinical Academic Group, St. George's University of London,
9	London, UK
10	
11	Word count: 1105 (including references and figure legend)
12	Author for correspondence: Professor Michael Papadakis, Consultant Cardiologist, St.
13	George's University of London, Cardiovascular Sciences, Cranmer Terrace, London, UK
14	E-mail: mipapada@sgul.ac.uk
15	
16	Conflict of interest: The authors have nothing to disclose.
17	Authorship: JB, GF and MP contributed to the conception or design of the work. JB, GF,
18	and MP contributed to the acquisition, analysis, or interpretation of data for the work.
19	JB drafted the manuscript. GF, CM, GP-W, HM, MT SS, MP critically revised the
20	manuscript. All gave final approval and agree to be accountable for all aspects of work
21	ensuring integrity and accuracy.
22	Funding: Dr Joyee Basu was funded by a research fellowship awarded by Cardiac Risk in
23	the Young.
24	Abbreviations: BA- black athlete, HCM-hypertrophic cardiomyopathy, LV-left ventricular,
25	LVH- left ventricular hypertrophy, LWMI- left ventricular mass index, RWT- relative wall
26	thickness, SCD-sudden cardiac death, WA- white athlete.
27	Ethnicity is a major determinant of cardiac adaptation to exercise. Black athletes (BAs)
28	demonstrate more profound electrical and structural changes, than white athletes (WAs),
29	which manifest on the 12-lead ECG and echocardiogram (1,2). It is well established that BAs
	© The Author(s) 2023. Published by Oxford University Press on behalf of the European Society of Cardiology. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com This article is published and distributed under the terms of the Oxford University Press, Standard Journals Publication Model

(https://academic.oup.com/pages/standard-publication-reuse-rights)

1

develop greater left ventricular hypertrophy (LVH) in response to exercise, compared to 1 WAs, creating a larger overlap between physiology and hypertrophic cardiomyopathy 2 3 (HCM). The issue is further compounded by the fact that BAs are at increased risk of exercise-related sudden cardiac death (SCD) with HCM accounting for a significant 4 proportion of cases (3). The growing number of elite black sportsmen and women has 5 intensified efforts to correctly identify those at risk. Left ventricular (LV) geometry has been 6 7 postulated as a more accurate tool compared to absolute LV wall thickness in differentiating physiological LV hypertrophy from HCM. Although LV geometry has been well 8 9 characterised in WAs (4) there is a paucity of data in male BAs and even less data in female BAs. This study aimed to establish the influence of black ethnicity on LV geometry and to 10 derive ethnicity-specific normative values for relative wall thickness (RWT). 11 12

This retrospective, cross-sectional cohort study included 640 BAs (80% male, mean age 22±5 13 years) and 1083 WAs (59% male, mean age 22±6 years) who underwent pre-participation 14 15 screening. Ethnicity was self-reported by each athlete. Athletes were assessed with a health questionnaire, ECG and echocardiogram. All athletes included in the study, were 16 asymptomatic, demonstrated a normal ECG and were free from cardiovascular disease. 17 Athletes participated in a variety of, predominantly mixed and dynamic, sporting disciplines 18 19 at regional and national level. In WAs, the most popular sports were swimming (11%), 20 cricket (9%), football (8%) and rowing (8%). In BAs the most popular sports were football (31%), athletics (25%) and boxing (9%). LV remodelling was categorised, based on RWT 21 and LVMI (left ventricular mass index), as normal, eccentric hypertrophy, concentric 22 23 remodelling or concentric hypertrophy (Figure 1). Results are presented as percentages for categorical data and mean±SD for continuous data. Reported upper thresholds were defined 24 as two SDs above the mean. Variables correlated with the dependent variable in univariate 25

analysis were entered into a multivariate model. Logistic regression analysis was used to
 determine the factors independently associated with LV remodelling. Ethical approval was
 granted by the National Research Ethics Service, Essex 2 and University Hospital Lewisham
 Research Ethics Committee in the United Kingdom.

5

21

Male athletes exhibited higher RWT (BAs: 0.37±0.07 vs 0.36±0.06; p=0.008, WAs 6 0.36±0.04 vs 0.35±0.04; p<0.001) and LVMI (BAs: 104.6±24g/m² vs 82.1±16.7g/m²; 7 p<0.001, WAs: 101 ± 21 g/m2 vs 83 ± 17 g/m²; p<0.001) compared to female athletes, across 8 both ethnicities. Male BAs demonstrated higher RWT (0.37±0.07 vs 0.36±0.04; p=0.002 and 9 LVMI (104.6±24g/m2 vs 101±21g/m2; p=0.02) than male WAs. In contrast, female BAs 10 exhibited higher RWT (0.36 ± 0.06 vs 0.35 ± 0.04 ; p=0.03 but similar LWMI (82.1 ± 16.7 g/m² vs 11 83 ± 17 g/m²; p=0.56) to female WAs. Most athletes demonstrated normal LV geometry 12 (Figure 1). Eccentric hypertrophy was present in 21% (n=91) of female WAs, 19% (n=125) 13 of male WAs, 17% (n=86) of male BAs and 14% (n=18) of female BAs. Concentric 14 15 remodelling or hypertrophy was present in 20% (n=102) male BAs, 12% (n=77) of male WAs, 9% (n=11) of female BAs and 7% (n=34) female WAs. In a multivariate model 16 (including age, gender, ethnicity and type of sport (static, dynamic and mixed sports), black 17 ethnicity was the only predictor of concentric remodelling or hypertrophy (OR 1.9, CI (1.5-18 2.6), p<0.001). The upper thresholds for RWT (two SDs above the mean) were: 0.51 for male 19 20 BAs, 0.48 for female BAs, 0.44 for male WAs and 0.43 female WAs.

This study shows that male BAs are more likely to exhibit concentric remodelling or
hypertrophy in comparison to white counterparts. It also provides important information
regarding cardiac remodelling in female BAs, who exhibit similar LV remodelling to male
BAs. A possible putative mechanism to explain differences in cardiac remodelling among

BAs and WAs is that of race related polymorphisms which may predispose to LVH (5). It is 1 also possible that there are quantitative and qualitative differences to the pattern of training 2 3 among BAs that may promote LVH. Our study was subject to the limitations of a single centre retrospective study. The findings would potentially not be applicable to older athletes 4 who may demonstrate a propensity to vascular rather than cardiac remodelling (6). Although 5 prevalence of hypertension in young athletes is low, blood pressure was not consistently 6 7 recorded across screening events. Moreover, BAs and WAs did not engage in the same type of sport and this may have determined at least partly the observed differences in LV 8 9 geometry. 10 In conclusion, one in five male BAs exhibit concentric remodelling or hypertrophy, with 11 significantly raised RWT and LVMI. Our findings suggest that in WAs, a RWT of >0.45, 12

13 commonly used as the upper limit of normal in clinical practice, should raise suspicion of

14 HCM. In contrast, a RWT of up to 0.51 for male and 0.48 for female BAs may be

15 physiological, and in the absence of symptoms, family history of HCM or premature SCD,

16 ECG abnormalities or additional echocardiographic indices, does not require further

- 17 investigations.
- 18

19 **References**

- Basavarajaiah S, Boraita A, Whyte G et al. Ethnic Differences in LV Remodeling in Highly-Trained Athletes. Relevance to Differentiating Physiologic LV Hypertrophy From Hypertrophic Cardiomyopathy. JACC 2008;51:2256–62.
 Sheikh N, Papadakis M, Carre F et al. Cardiac adaptation to exercise in adolescent athletes of African ethnicity: An emergent elite athletic population. Br J Sports Med
- athletes of African ethnicity: An emergent elite athletic population. Br J Sports Med
 2013;47:585–92.
- Harmon KG, Drezner JA, Wilson MG et al. Incidence of sudden cardiac death in athletes: A state-of-the-art review. Br J Sports Med 2014:1185–92.
- Finocchiaro G, Dhutia H, D'Silva A et al. Effect of Sex and Sporting Discipline on LV Adaptation to Exercise. JACC Cardiovasc Imaging 2017;10:965–72.

- Pauliks LB, Cole KE, Mergner WJ. Increased insulin-like growth factor-1 protein in human LV hypertrophy. Exp Mol Pathol 1999;66(1):53–8.
- Torlasco C, D'Silva A, Buva AN et al. Age matters: differences in exercise-induced
 cardiovascular remodelling in young and middle aged healthy sedentary individuals.
 EJPC 2020;28(7): 738-746.
 - В Α FEMALES MALES Eccentric hypertrophy Concentric hypertrophy Eccentric hypertrophy Concentric hypertrophy 220 22 20 200 18(180 160 160 14(140 LVMI IVMI 120 100 80 Normal Concentric remodelling Normal Concentric remodelling RΔ< RWT RWT WAs С 100 % 30 20 10 0 Male BA Male WA Female BA Female WA Male BA Female BA Female WA Male WA Dynamic Mixed Concentric Remodelling Eccentric Hypertrophy Concentric Hypertrophy Normal

6

7

- **1 Figure 1.** Distribution of LV geometry types in white and black, male (A) and female (B) athletes. Black
- 2 individuals are represented by a square, and white individuals by a circle. The red lines on each graph
- 3 correspond to normal RWT (<0,42) and LVMI ($<95g/m^2$ in women and $<115g/m^2$ in men) values (Lang R et al.
- 4 Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the
- 5 ASE and the EACVI. Eur Heart J Cardiovasc Imaging 2015;16:233-271). RWT= relative wall thickness,
- LVMI= left ventricular mass index. (C) LV geometry in black and white athletes according to dynamic or mixed
 sports participation. BA= black athletes, WA= white athletes.
- 8

9 Data availability statement

- 10 The data underlying this article cannot be shared publicly due to the privacy of individuals
- 11 that participated in the study. The data will be shared on reasonable request to the
- 12 corresponding author.